[77670/495]

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Reissue Applicant	:	Hiroyuki Nakane, Chikara Ohto, Shinichi Ohnuma, Kazutake Hirooka, Tokuzo Nishino
Reissue Serial No.	:	To be Assigned
Reissue Application Filed	:	Herewith
Patent No.	:	5,935,832
Issued	:	August 10, 1999
Title	:	FARNESYL DIPHOSPHATE SYNTHASE
Examiner	:	To be Assigned
Art Unit	:	To be Assigned

Box REISSUE
Assistant Commissioner for Patents
Washington, D.C. 20231

REISSUE DECLARATION AND POWER OF ATTORNEY

We, Hiroyuki Nakane, Chikara Ohto, Shinichi Ohnuma, Kazutake Hirooka and Tokuzo Nishino, hereby declare as follows:

1. We believe that we are the original, first and sole inventors of the invention described and claimed in United States Letters Patent No. 5,935,832 ("the '832 patent"), entitled FARNESYL DIPHOSPHATE SYNTHASE, which issued on August 10, 1999. A copy of the '832 patent is attached at Tab A.

2. We respectfully request that a reissue patent be issued of the '832 patent. New claims, and amendments to the specification and claims of the '832 patent are provided below. An explanation of the amendments, added claims and the support therefor is also provided in this Declaration.

3. We declare that we have reviewed and understand the contents of the '832 patent, the issued claims, the amended specification, and the new and amended claims.

4. We acknowledge the duty to disclose information that is material to patentability of the new and amended claims as defined in Title 37, Code of Federal Regulations, § 1.56(a).

5. The '832 patent issued from U.S. Application Ser. No. 08/898,560, filed July 22, 1997. We hereby claim the benefit under Title 35, United States Code, Section 119 and/or Section 120 of the Japanese application listed below.

Foreign Application Priority Information:

Serial No.	**Filing Date**
Japan 8-213211	Jul.24, 1996

Insofar as the subject matter of each of the claims of this application is not disclosed in this Japanese application in the manner provided by the first paragraph of Title 35, United States Code, Section 112, we acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, Section 1.56(a) that occurred between the filing date of the prior Japanese application and the filing date of U.S. Application Serial No. 08/898,560.

6. We believe the original patent to be partly inoperative because of inadvertant error that arose without deceptive intent and that resulted in our claiming less than we had a right to claim.

7. Upon re-evaluation of the issued claims of the '832 patent, it was realized that, through inadvertant error, applicants claimed less than they had a right to claim. Therefore, applicants believe that the '832 patent is wholly or partially inoperative by reason of patentee claiming less than the patentee

had a right to claim in the patent.[1] In particular, independent claim 1 of the '832 patent is directed to a mutant prenyl diphosphate synthase which can have an amino acid substitution located one position upstream of D_3. However, certain advantageous embodiments of the invention that are disclosed in the '832 patent specification are not, through inadvertant error, specifically claimed in the '832 patent. For example, particular mutant prenyl diphostate synthases which have an amino acid substitution "located two positions upstream of D_3" are described in the specification but the claims of the '832 patent do not explicitly include this language. Accordingly, newly added claims 19-34 are presented in this reissue application to clarify the patent coverage to which Applicants are entitled.

8. The newly added claims and the support therefor are set forth as follows for the examiner's convenience.

Claim 19. A mutant prenyl diphosphate synthase having a modified amino acid sequence, wherein

said mutant diphosphate synthase comprises an aspartic acid-rich domain having the sequence, $D_1D_2X_1(X_2X_3)X_4D_3$, in region II of said mutant prenyl diphosphate synthase,

wherein each of D_1, D_2, and D_3 denote an aspartic acid residue; X_1, X_2, X_3, and X_4 are each independently any amino acid and X_2 and X_3 are each optionally independently present in the aspartic acid rich domain, and wherein

said mutant prenyl disphosphate synthase comprises (1) at least one amino acid substitution, said at least one amino acid substitution located at least one amino acid position selected from (a) an amino acid between D_1 and the amino acid residue at the fifth position upstream of D_1 and (b) the amino acid residue located one amino acid

[1] It is respectfully noted that this reissue application is being filed within two years of issuance of the '832 patent.

position downstream of D_2; (2) at least one additional amino acid inserted between the first amino acid downstream of D_2 and the first amino acid upstream of D_3; or (3) a combination of (1) and (2);

wherein said mutant prenyl diphosphate synthase synthesizes prenyl diphosphate which is shorter than prenyl diphosphate synthesized by a corresponding wild-type enzyme.

Applicants submit that they are entitled to subject matter relating to "(b) the amino acid residue located one amino acid position downstream of D_2" because this subject matter is distinct from that of Claim 1 and mutant enzymes containing mutations located one amino acid position downstream of D_2 are described in the specification.

As taught by the specification, a position located one amino acid position downstream of D_2 is position 84 in the wild type *Sulfolobus acidocaldarius* enzyme (*compare* the formula $D_1D_2X_1(X_2\ X_3)X_4\ D_3$ with the Feature identified by SEQ ID NO: 1). The specification teaches that the isoleucine present at position 84 (X_1) in the wild type *Sulfolobus acidocaldarius* enzyme can, according to the present invention, be substituted with another amino acid. *See* '832 Patent, Col. 6, lines 35-44; Examples 2 and 4. In "Mutant enzyme 5", the specification teaches that leucine can be substituted for the isoleucine at position 84. *See* '832 Patent, Col. 6, lines 59-64; *see also* SEQ ID NOS: 13 and 8 (showing that a codon for isoleucine (ATT and ATC) can be replaced with a codon for leucine (CTT)).

Furthermore, the specification teaches that amino acids can be inserted between amino acid position 84 (X_1) and amino acid position 85 (X_4). In "Mutant enzyme 5", the specification teaches insertion of a proline (X_2) and serine (X_3) residue in between the isoleucine at position 84 (X_1) and the methionine at position 85 (X_4). Accordingly, Applicants submit that the subject matter of Claim 19 is fully supported by the specification and that no new subject matter is being presented in this reissue application.

Claims 20-34 depend from independent Claim 19 and relate to the subject matter of issued claims 2-16. Accordingly, Applicants submit that the subject matter of these claims is fully also supported by the specification and that no new subject matter is being presented in this reissue application.

Claim 20. A mutant prenyl diphospate synthase according to claim 19 wherein said mutant has the enzymatic activities and thermostability of wild type prenyl diphosphate synthase.

Claim 21. A mutant enzyme according to claim 19 wherein the reaction product of the prenyl diphosphate synthase is farnesyl diphosphate.

Claim 22. A mutant enzyme according to claim 19 wherein the prenyl diphosphate synthase is a homodimer.

Claim 23. A mutant enzyme according to claim 19 wherein the prenyl diphosphate synthase is derived from archaea.

Claim 24. A mutant enzyme according to claim 19 wherein the prenyl diphosphate synthase is derived from *Sulfolobus acidocaldarius*.

Claim 25. A mutant enzyme according to claim 19 wherein the prenyl diphosphate synthase is a thermostable enzyme.

Claim 26. A mutant prenyl diphosphate synthase according to claim 19, wherein at least one amino acid selected from phenylalanine at position 77, threonine at position 78, valine at position 80, histidine at position 81, and isoleucine at position 84 has been substituted by another amino acid, or one or more amino acids have been inserted in between isoleucine at position 84 and methionine at position 85 in the geranylgeranyl diphosphate synthase as set forth in SEQ ID No:1.

Claim 27. A mutant prenyl diphosphate synthase according to claim 19 wherein at least one amino acid selected from phenylalanine at position 77, threonine at position 78, valine at position 80, histidine at position 81, and isoleucine at position 84 has been substituted by another amino acid, and/or two amino acids have been inserted between isoleucine at position 84 and methionine at position 85 in the geranylgeranyl diphosphate synthase as set forth in SEQ ID No: 1, wherein the phenyl alanine at position 77 has been replaced with tyrosine, the threonine at position 78 has been replaced with phenylalanine or serine, the valine at position 80 has been replaced with isoleucine, the histidine at position 81 has been replaced with leucine or alanine, or the isoleucine at position 84 has been replaced with leucine; or proline and serine have been inserted in between the isoleucine at position 84 and the methionine at position 85.

Claim 28. A mutant prenyl diphosphate synthase according to claim 19, wherein the mutant prenyl diphosphate synthase is derived from a native geranylgeranyl diphosphate synthase of an organism selected from the group consisting of *Arabidopsis thaliana, Lupinas albus, Capsicum annuum, Sulfolobus acidocaldarius, Rhodobactor sphaeroides, Rhodobacter capsulatus, Erwinia herbicola, Myxococcus thaliana and Neurospora crassa.*

Claim 29. A DNA encoding an enzyme according to claim 19.

Claim 30. An RNA transcribed from a DNA according to claim 29.

Claim 31. A recombinant vector comprising a DNA according to claim 29.

Claim 32. A host organism transformed with a recombinant vector according to claim 31.

Claim 33. A process for producing a mutant enzyme according to claim 19, said method comprising the steps of culturing a host transformed with an

expression vector comprising a DNA coding for the mutant enzyme and harvesting the expression product from the culture.

Claim 34. A process for producing a prenyl diphosphate having not more than 15 carbons comprising the step of bringing an enzyme according to claim 19 into contact with a substrate selected from the group consisting of isopentenyl diphosphate, dimethylallyl diphosphate, and geranyl diphosphate.

9. Inadvertant typographical errors are present in the '832 specification and in issued Claim 1 of the '832 patent. These errors are corrected in the amendments provided below.

A. At col. 1, line 15, please delete the "s" from "unit[s]". The paragraph containing this text is reproduced below, with the correction identified.

> Of the substances having important functions in organisms, many are biosynthesized using isoprene (2-methyl-1,3-butadiene) as a constituent unit[s]. These compounds are also called isoprenoids, terpenoids, or terpenes, and are classified depending on the number of carbon atoms into hemiterpenes (C5), monoterpenes (C10), sesquiterpenes (C15), diterpenes (C20), sesterterpenes (C25), triterpenes (C30), tetraterpenes (C40), and the like. The actual biosynthesis starts with the mevalonate pathway through which mevalonic acid-5-diphosphate is synthesized, followed by the synthesis of isopentenyl diphosphate (IPP) which is an active isoprene unit.

B. At col. 1, line 45, please delete the "plants" and at col. 1, line 46, after "in" please insert "plants." The paragraph containing this text is reproduced below, with the corrections identified.

There are Z type and E type condensation reactions. Geranyl diphosphate is a product of E type condensation and neryl diphosphate is of Z type condensation. Although, the all-E type is considered to be the active form in farnesyl diphosphate and geranylgeranyl diphosphate, the Z type condensation reaction leads to the synthesis of natural rubber, dolichols, bactoprenols (undecaprenols), and [plants] various polyprenols found in plants. They are believed to undergo the condensation reaction using the phosphate ester bond energy of the pyrophosphate and the carbon backbone present in the molecule and to produce pyrophosphate as the byproduct of the reaction.

C. At col. 2, line 4, please delete "[geraniols and that isomer nerol belonging]" and substitute "geraniol and its isomer, nerol, belonging" therefor. At col. 2, line 5, after "monoterpens" please insert "that." The paragraph containing this text is reproduced below, with the corrections identified.

Furthermore, via the biosynthesis of these active-form isoprenoids, a vast number of kinds of compounds that are vital to life have been synthesized. Just to mention a few, there are cytokinins that are plant hormones and isopentenyl adenosine-modified tRNA that use hemiterpenes as their precursor of synthesis, [geraniols and that isomer nerol belonging] geraniol and its isomer, nerol, belonging to monoterpens that are the main components of rose oil perfume and a camphor tree extract, camphor, which is an insecticide. Sesquihormones include juvenile hormones of insects,

diterpenes include a plant hormone gibberellin, trail pheromones of insects, and retinols and retinals that function as the visual pigment precursors, binding components of the purple membrane proteins of highly halophilic archaea, and vitamin A.

D. At col. 3, line 45, please delete "[(DDXX(XX)D)]" and substitute "$\underline{(D_1D_2X_1(X_2X_3)X_4D_3)}$" therefore. At col. 3, line 56, please delete the "[have not been]" and substitute "<u>are</u>" therefor. At col. 3, line 57, please delete the "[that induce mutation]" and substitute "<u>that include mutations</u>" therefor. At col. 3, lines 58-59, please delete "[to be in the short chain-length side]" and substitute with <u>having a shorter chain length</u>. The paragraph containing this text is reproduced below, with the corrections identified.

> It has been found out that of the two aspartic acid-rich domains that have been proposed based on the amino acid sequence of the prenyl diphosphate synthase, the amino acid residue located at the fifth position in the N-terminal direction from the conserved sequence I [(DDXX(XX)D)] $\underline{(D_1D_2X_1(X_2X_3)X_4D_3)}$ (wherein X denotes any amino acid, and the two X's in the parentheses may not be present) of the aspartic acid-rich domain in the amino-terminal side is responsible for controlling the chain length of the reaction product. Hence, a method has been invented that controls the reaction product for the purpose of lengthening the chain length of the reaction product [Japanese patent application No. 8-191635 filed on Jul. 3, 1996 under the title of "A Mutant Prenyl Diphosphate Synthase"]. The enzyme produced using the method enables production of reaction products that have several chain lengths. However, methods

[have not been] are not known [that induce mutation] that include mutation of geranylgeranyl diphosphate synthase to control the reaction products [to be in the short chain-length side] having a shorter chain length in order to produce farnesyl diphosphate.

E. At col. 4, line 2, please delete the "[owned by the]" and substitute "exhibited by" therefor. The paragraph containing this text is reproduced below, with the corrections identified.

It is an object of the invention to establish a process for producing farnesyl diphosphate synthases by modifying amino acid sequences of prenyl diphosphate enzymes. A new enzyme that is more stable or that has a high specific activity more adaptable to industrial application would make it possible to obtain immediately a mutant prenyl diphosphate synthase or the gene thereof that produces farnesyl diphosphate and that retains the property [owned by the] exhibited by the prenyl diphosphate synthase prior to mutation.

F. At col. 4, line 11, please delete "[(DDXX(XX)D)]" and substitute "$(D_1D_2X_1(X_2X_3)X_4D_3)$" therefore. The paragraph containing this text is reproduced below, with the corrections identified.

From the information on the nucleotide sequence of the gene of the geranylgeranyl diphosphate synthase of the mutant Sulfolobus acidocaldarius (S. acidocaldarius), it was clarified that out of the two Aspartic acid-rich domains that have been proposed based on the analysis of the amino acid sequence of prenyl diphosphate synthases, the amino acid residues within the aspartic

acid-rich domain conserved sequence I [(DDXX(XX)D)] $\underline{(D_1D_2X_1(X_2X_3)X_4D_3)}$ at the amino terminal side or the five amino acid residues to the N-terminal side from the amino terminal of said conserved sequence I are involved in the control of chain length of the reaction products.

G. At col. 4, line 23, please delete "[(DDXX(XX)D)]" and substitute "$\underline{(D_1D_2X_1(X_2X_3)X_4D_3)}$" therefor. At col. 4, line 26, please delete "[at the position in the N-terminal direction from D of the C-terminal of said aspartic acid-rich domain]" and substitute "<u>one amino acid position downstream of D2</u>" therefor. The paragraph containing this text is reproduced below, with the corrections identified.

> at least one amino acid residue selected from (a) the amino acid residues in between the amino acid residue located at the fifth position in the N-terminal direction from D of the N-terminal and the amino acid residue located at the first position in the N-terminal direction from D of said N-terminal of the aspartic acid-rich domain [DDXX(XX)D] $\underline{(D_1D_2X_1(X_2X_3)X_4D_3)}$ (wherein X sequence denotes any amino acid, and the two X's in the parentheses may not be present) present in region II, and (b) the amino acid residue located <u>one amino acid position downstream of D2</u> [at the position in the N-terminal direction from D of the C-terminal of said aspartic acid-rich domain] has been substituted by another amino acid, and/or

H. At col. 4, line 32, please delete "[amino acid residues located at the first position in the N-terminal direction from D of the C-terminal and D

of said C-terminal]" and substitute "first amino acid downstream of D_2 and the first amino acid upstream of D_3." therefor. The paragraph containing this text is reproduced below, with the corrections identified.

> additional amino acid(s) have been inserted in between the first amino acid downstream of D_2 and the first amino acid upstream of D_3 [amino acid residues located at the first position in the N-terminal direction from D of the C-terminal and D of said C-terminal] of said aspartic acid-rich domain.

I. At col. 5, line 36, please delete "[(DXX(XX)D)]" and substitute "$(D_1D_2X_1(X_2X_3)X_4D_3)$" therefore. The paragraph containing this text is reproduced below, with the corrections identified.

> It has been proposed that there are five conserved regions in the amino acid sequence of a prenyl diphosphate synthase (one subunit in the case of a heterodimer) [A. Chem et al., Protein Science Vol. 3, pp. 600-607, 1994]. It is also known that of the five conserved regions, there is an aspartic acid-rich domain conserved sequence I [[DDXX(XX)D]] $D_1D_2X_1(X_2X_3)X_4D_3$ (wherein X denotes any amino acid, and the two X's in the parentheses may not be present) in region II. Although there is also an aspartic acid-rich domain indicated as "DDXXD" in region V, the aspartic acid-rich domain used to specify the modified region of the amino acid sequence of the present invention is the one present in region II, and this domain is termed as the aspartic acid-rich domain I as compared to the aspartic acid-rich domain II present in region V.

J. At col. 6, line 6, please delete "[(DDXX(XX)D)]" and substitute "$\underline{(D_1D_2X_1(X_2X_3)X_4D_3)}$" therefore. At col. 6, line 8, please delete "[at the position in the N-terminal direction from D of the C-terminal of said aspartic acid-rich domain]" and substitute "<u>one amino acid position downstream of D2</u>" therefor. The paragraph containing this text is reproduced below, with the corrections identified.

> In accordance with the present invention, in the amino acid sequence of a prenyl diphosphate synthase, at least one amino acid residue selected from (a) the amino acid residues in between the amino acid residue located at the fifth position in the N-terminal direction from D of the N-terminal and the amino acid residue located at the first position in the N-terminal direction from D of said N-terminal of the aspartic acid-rich domain [DDXX(XX)D] $\underline{D_1D_2X_1(X_2X_3)X_4D_3}$ (wherein X sequence denotes any amino acid, and the two X's in the parentheses may not be present) present in region II, and (b) the amino acid residue located <u>one amino acid position downstream of D2</u> [at the position in the N-terminal direction from D of the C-terminal of said aspartic acid-rich domain] has been substituted by another amino acid, and/or

K. At col. 6, line 16, lease delete "[amino acid residues located at the first position in the N-terminal direction from D of the C-terminal and D of said C-terminal]" and substitute "<u>first amino acid downstream of D_2 and the first amino acid upstream of D_3</u>" therefor. The paragraph containing this text is reproduced below, with the corrections identified.

> an additional amino acid(s) have been inserted in between the <u>first amino acid downstream of D_2 and the first amino acid upstream of D_3</u> [amino acid residues

located at the first position in the N-terminal direction from D of the C-terminal and D of said C-terminal] of said aspartic acid-rich domain.

L. At col. 7, line 67, please delete "[biding]" and substitute "binding" therefor. The paragraph containing this text is reproduced below, with the corrections identified.

> It is known that the distance between the sequence of the ribosome [biding] binding site (GGAGG and similar sequences thereof) and the initiation codon ATG is important as the sequence regulating the ability of synthesizing protein from mRNA. It is also well known that a terminator (for example, a vector containing rrn PT_1 T_2 is commercially available from Pharmacia) that directs transcription termination at the 3'-end affects the efficiency of protein synthesis by a recombinant.

M. At col. 9, line 14, please delete "[a]" and substitute "an" therefor. At col. 9, line 16, please delete "[prrenyl]" and substitute "prenyl" therefor. The paragraph containing this text is reproduced below, with the correction identified.

> By using the method of producing the mutant prenyl diphosphate synthase obtained by the present invention, the mutant prenyl diphosphate synthase derived from [a] an archaea may be created that is more stable and thus easier to handle and that produces [prrenyl] prenyl diphosphate. Furthermore, there is also expected a creation of the farnesyl diphosphate-producing mutant prenyl diphosphate synthase that has the property of the prenyl diphosphate synthase prior to mutation (for

example, salt stability or stability in a wide range of pH) added thereto.

N. At col. 10, line 4, please delete "[Geranylaeranyl]" and substitute "Geranylgeranyl" therefor. The paragraph containing this text is reproduced below, with the corrections identified.

Construction of a Plasmid Containing the Gene for [Geranylaeranyl] Geranylgeranyl Diphosphate Synthase

O. At col. 10, line 57, please delete "[TATT-31]" and substitute "TATT-3' " therefor. The paragraph containing this text is reproduced below, with the corrections identified.

Introduction of the mutation (F77Y, T78S, V80I, I84L, 84PS85) was effected using two nucleotides. First, mutation was introduced as mentioned in Example 3 using the oligonucleotide
5'-GTTCTTCATACTTATTCGCTTATTCATGATAG
[TATT-31] TATT-3' (SEQ ID No: 7) and a transformant was prepared in accordance with Example 4, and furthermore mutation was introduced into the plasmid thus obtained using the oligonucleotide
5'-ATTCATGATGATCTTCCATCGATGGATCAAGAT-3'
(SEQ ID No: 8).

P. At col. 11, line 24, please delete "[H2O]" and substitute "H_2O " therefor. The paragraph containing this text is reproduced below, with the corrections identified.

[H2O] H_2O 5 µl

Q. At col. 11, line 56, please delete "[H2O]" and substitute "$\underline{H_2O}$ " therefor. The paragraph containing this text is reproduced below, with the corrections identified.

[H2O] $\underline{H_2O}$ make to a final volume of 10 µl

R. At col. 12, line 35, please delete "[ATATCATG-31]" and substitute "ATATCATG-3' " therefor. The paragraph containing this text is reproduced below, with the corrections identified.

F77Y, T78F, H81L: 5'-TATTTCCTTGTGCTTGATG
[ATATCATG-31] ATATCATG-3' (SEQ ID No: 11)

10. Amended Claim 1 also contains inadvertant typographical errors which are corrected as set forth below.

1. A mutant prenyl diphosphate synthase having a modified amino acid sequence, wherein

said mutant diphosphate synthase comprises an aspartic acid-rich domain having the sequence, $D_1D_2X_1X_2(X_3X_4)D_3$, in region II of said mutant prenyl diphosphate synthase,

wherein each of D_1, D_2, and D_3 denote an aspartic acid residue; X_1, X_2, X_3, and X_4 are each independently any amino acid and X_3 and X_4 are each optionally independently present in the aspartic acid rich domain, and wherein

said mutant prenyl disphosphate synthase comprises (1) at least one amino acid substitution, said at least one amino acid substitution located at at least one amino acid position selected from (a) an amino acid between D_1 and the amino acid residue at the fifth position upstream of D_1 and (b) the amino acid residue located one amino acid

positions upstream of D_3; (2) at least one additional amino acid inserted between D_3 and the first amino acid upstream of D_3; or (3) a combination of (1) [(2)] and (2) [(3)];

wherein said mutant prenyl diphosphate synthase synthesizes prenyl diphosphate which is shorter than prenyl diphosphate synthesized by a corresponding wild-type enzyme.

11. All errors that are being corrected in the present reissue application up to the time of filing of this declaration arose without any deceptive intention on the part of the applicants.

12. We hereby offer to surrender the original patent upon reissue of the patent.

13. We declare that Toyota Jidosha Kabushiki Kaisha is the assignee for the '832 patent and have attached a copy of the assignment (recorded at the United States Patent and Trademark Office at reel 8647, frame 0509) at Tab B. As provided by the statement attached at Tab C, Toyota Jidosha Kabushiki Kaisha assents to the filing of this reissue application, and confirms the reissue applicants' offer to surrender the original '832 patent as stated in the previous paragraph.

14. We hereby appoint the following practitioners to prosecute this application and transact all business in the Patent and Trademark Office connected therewith:

Estelle Tsevdos (Reg. No. 31145)
Judith L. Toffenetti (Reg. No. 39048)

15. Please direct all correspondence and telephone calls to:

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16. Our residence addresses, post office addresses and countries of citizenship are stated below next to our names.

17. We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

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Ref : TYT-E150-0

U.S. ASSIGNMENT

IN CONSIDERATION of the sum of One Dollar ($1.00), and of other good and valuable consideration paid to the undersigned inventor(s) (hereinafter "ASSIGNOR") by

(Insert ASSIGNEE's Name(s) Address(es))

TOYOTA JIDOSHA KABUSHIKI KAISHA
1, Toyota-cho, Toyota-shi, Aichi, Japan

(hereinafter "ASSIGNEE"), the receipt of which is hereby acknowledged, the undersigned ASSIGNOR hereby sells, assigns and transfers to ASSIGNEE the entire and exclusive right, title and interest to the invention entitled

(Title of Invention)

FARNESYL DIPHOSPHATE SYNTHASE

relating to International Patent Application PCT/JP _____/_____ and/or for which application for Letters Patent of the United States was executed on even date herewith or, if not so executed, was:

(Insert date of execution of application, if not concurrent)

(a) executed on _____;

(b) filed on _____, Serial No. _____/_____;

(_____ _____ _____) is hereby authorized to insert in (b) the specified data, when known.

and to said application and all Letters Patent(s) of the United States granted on said application and any continuation, division, renewal, substitute, reissue or reexamination application based thereon, for the full term or terms for which the said Letters Patent(s) may be granted and including any extensions thereof (collectively, hereinafter, "said application(s) and Letters Patent(s)").

The ASSIGNOR agree(s), when requested by said ASSIGNEE and without charge to but at the expense of said ASSIGNEE, to do all acts which the ASSIGNEE may deem necessary, desirable or expedient, for securing, maintaining and enforcing protection for said invention, including in the preparation and prosecution of said application(s) and the issuance of said Letters Patent(s), in any interference, reissue, reexamination, or public use proceeding, and in any litigation or other legal proceeding which may arise or be declared in relation to same, such acts to include but not be limited to executing all papers, including separate assignments and declarations, taking all rightful oaths, providing sworn testimony, and obtaining and producing evidence.

IN WITNESS WHEREOF, the undersigned inventor(s) has (have) affixed his/her/their signature(s).

(Signatures)

	(SIGNATURE)	(TYPE NAME)	(DATE)
1)	Hiroyuki Nakane	Hiroyuki Nakane	June 20, 1997
2)	Chikara Ohto	Chikara Ohto	June 20, 1997
3)	Shinichi Ohnuma	Shinichi Ohnuma	June 20, 1997
4)	Kazutake Hirooka	Kazutake Hirooka	June 20, 1997
5)	Tokuzo Nishino	Tokuzo Nishino	June 20, 1997

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ASSENT BY ASSIGNEE

Toyota Jidosha Kabushiki Kaisha, which is the assignee of the entire right, title and interest in United States Patent No. 5,935,832, entitled FARNESYL DIPHOSPHATE SYNTHASE, which assignment is recorded in the records of the United States Patent and Trademark Office at reel 8647, frame 0509, hereby assents to the filing of the reissue application for said Patent No. 5,935,832 that is attached to this Declaration, and confirms reissue applicants' offer to surrender the original '832 patent as stated therein, and to the appointment of power of attorney as stated therein.

TOYOTA JIDOSHA KABUSHIKI KAISHA

Date: June 12, 2001

Name: Masahiro Ezaki

Title: General Manager, Intellectual Property Division